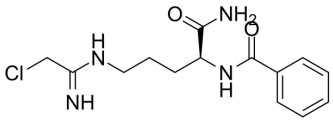
Cl-amidine

Cat. No.:	HY-100574
CAS No.:	913723-61-2
Molecular Formula:	$C_{14}H_{19}ClN_4O_2$
Molecular Weight:	310.78
Target:	Protein Arginine Deiminase; Apoptosis; MicroRNA
Pathway:	Epigenetics; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Cl-amidine is an orally active peptidylarginine deminase (PAD) inhibitor, with IC_{50} values of 0.8 μM, 6.2 μM and 5.9 μM for PAD1, PAD3, and PAD4, respectively. Cl-amidine induces apoptosis in cancer cells. Cl-amidine induces microRNA (miR)-16 (miRNA-16, microRNA-16) expression and causes cell cycle arrest. Cl-Amidine prevents histone 3 citrullination and neutrophil extracellular trap formation, and improves survival in a murine sepsis model[1][2][3][4][5].

IC_{50} & Target

IC50: 0.8 μM (PAD1), 5.9 μM (PAD4), 6.2 μM (PAD3)[1][5].

In Vitro

Cl-amidine is a bioavailable haloacetamidine-based compound that inhibits all the active PAD isozymes with near equal potency (k_{inact}/K_I=13,000 M_{-1}•min-1 for PAD4)[1].

Cl-amidine (0, 5, 10, 15, 20, 25, 50 μg/mL, 24 hours) induces apoptosis in TK6 lymphoblastoid cells and HT29 colon cancer cells in a dose-dependent manner. Interestingly, the colon cancer cell line (HT29) is relatively resistant to apoptosis caused by Cl-amidine[2].

Cl-amidine irreversibly inactivates PADs by covalently modifying an active site cysteine that is important for its catalytic activity[4].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Apoptosis Analysis[2].

Cell Line:	TK6 lymphoblastoid cells and HT29 colon cancer cells.
Concentration:	0, 5, 10, 15, 20, 25, 50 μg/mL.
Incubation Time:	24 h.
Result:	Induced apoptosis dose-dependently.

In Vivo

Cl-amidine (75 mg/kg, ip once daily) suppresses and treats DSS-induced colitis in mice[2].

Cl-amidine (5, 25, 75 mg/kg, oral gavage, once daily) leads to significant reductions in the histology scores dose-dependently[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	C57BL/6 mice (8-12 wk old, DSS mouse model of colitis)[2].
Dosage:	75 mg/kg.

Administration:	IP once daily.
Result:	Suppressed PAD activity, protein citrullination, and PAD levels in the colon in vivo.

Animal Model:	C57BL/6 mice (8-12 wk old, DSS mouse model of colitis)[2].
Dosage:	5, 25, 75 mg/kg.
Administration:	Oral gavage once daily.
Result:	Led to significant reductions in the histology scores.

CUSTOMER VALIDATION

- Cell Rep. 2021 Sep 21;36(12):109750.
- Neoplasia. 2022 Nov;33:100835.
- Transl Res. 2022 Nov 23;S1931-5244(22)00252-3.
- Fish Shellfish Immunol. 2022 Aug 3;S1050-4648(22)00414-4.
- Chem Res Toxicol. 2022 Feb 15.

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REFERENCES

[1]. Yuan Luo, et al. Inhibitors and Inactivators of Protein Arginine Deiminase 4: Functional and Structural Characterization. Biochemistry. 2006 Oct 3; 45(39): 11727–11736.

[2]. Chumanevich AA, et al. Suppression of colitis in mice by Cl-amidine: a novel peptidylarginine deiminase inhibitor. Am J Physiol Gastrointest Liver Physiol. 2011 Jun;300(6):G929-38.

[3]. Witalison EE, et al. Molecular targeting of protein arginine deiminases to suppress colitis and prevent colon cancer. Oncotarget. 2015 Nov 3;6(34):36053-62.

[4]. Biron BM, et al., Cl-Amidine Prevents Histone 3 Citrullination and Neutrophil Extracellular Trap Formation, and Improves Survival in a Murine Sepsis Model. J Innate Immun. 2017;9(1):22-32.

[5]. Bryan Knuckley, et al. Substrate Specificity and Kinetic Studies of PADs 1, 3, and 4 Identify Potent and Selective Inhibitors of Protein Arginine Deiminase 3. Biochemistry. 2010 Jun 15;49(23):4852-63.

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